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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/426,548

10/22/99

ROBBINS

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DEX-0054

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HM12/1002

EXAMINER

WDITACH, J

ART UNIT

PAPER NUMBER

1632

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18
10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/426,548

Applicant(s)

ROBBINS ET AL.

Examiner

Joseph Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Continued Prosecution Application

The request filed on July 5, 2001, paper number 17, for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/426,548 is acceptable and a CPA has been established. An action on the CPA follows.

This is an original application filed October 20, 1999 which claims benefit to provisional application 60/105,180, filed October 22, 1998.

As requested in the filing of the CPA, Applicants' amendments filed April 9, 2001, paper number 12, and May 14, 2001, paper number 14 have been entered. Claims 1-3 have been amended. Claims 1-3 are pending and currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, in claim 1

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the recitation of 'GenBank Accession Nos. U07418 and U03911' finds neither literal nor figurative support in the specification. Applicants point to page 1 of the specification where Examiner only finds citations of references which have not been made of record. Upon further review of the entire specification and the art of record, the Examiner was unable to find the recitation of these specific GenBank Accession numbers. The instant specification describes the specific polymorphisms in the MLH and MSH gene in reference to the specific exon or intron in which they are present. The sequences for the introns and exons are set forth in the specification (pages 4-15), and the specific mutations in said sequences are set forth in Table I. Support for the correlation of the mutations to hereditary non-polyposis colorectal cancer is set forth on pages 15-17 and Example 4. The only support for the specific mutations is within the context of the specific base pair changes in the corresponding SEQ ID NOs. In addition, a review of the sequences set forth in GenBank Accession NOs. U07418 and U03911 indicates that these sequences represent the coding sequence, and as such, provide no teaching or support for intron or exon borders. Further, it provides no support for the IVS mutation because this resides in the intron sequence.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1-3 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

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MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure*" (emphasis added).

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published on December 12, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

The specification fails to provide the necessary details to adequately define a variant human MLH1 or MSH2 gene. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991),

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clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed " Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116. The instant specification describes the specific polymorphisms in the MLH and MSH gene in reference to the specific exon or intron in which they are present. The sequences for the introns and exons are set forth in the specification (pages 4-15), and the specific mutations in said sequences are set forth in Table I. The only support for the specific mutations is within the context of the specific base pair changes in the corresponding SEQ ID NOs. The sequences set forth in GenBank Accession NOs. U07418 and U03911 provide a description of the coding sequence for these genes, however the sequences provide no teaching or support for intron or exon borders or other elements present in these genes. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). Examiner agrees that the specific polymorphisms described in the specification can be correlated to hereditary non-

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polyposis colorectal cancer. However, the claims encompass the entire gene and the skilled artisan cannot envision what other changes exist or can be made to the nucleic acid sequences encompassed by a variant gene. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or identifying it. See *Piers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). It would be difficult for one of skill in the art to imagine the many sequences encompassed by the breadth of the claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is indefinite in the recitation of 'GenBank Accession NOs. U07418 and U03911' because GenBank represents a computer database which is subject to continuous updates and modifications. Thus, the sequences defined by these accession numbers is subject to change. For example, the NCBI listing supplied by Applicant in the After final amendment filed May 14, 2001, paper number 14, indicates that the file for hMSH2 has already been modified at least once replacing gi:439404 (see comment section). Defining and claiming the specific mutations as

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comprising the specific base pair change in the corresponding SEQ ID NO would obviate the basis of the rejection.

Further, claim 1 is vague and indefinite in the recitation of a 'variant human MLH1 or MSH2 gene' because these genes have not been completely defined. The specification provides the necessary sequences to define the intron/exon borders and the complete exon, however there is no teaching for the complete intron. Further, other sequences encompassed by a gene such as the promoters and transcriptional elements are not defined nor described. In addition, the specific mutations are defined by the position of the mutation in the 'wild type/normal' gene sequence, and in the context of a gene from a particular patient(s). There is no teaching to the structure of the gene or other mutations which may be present in said gene in said patient. The artisan would be unaware of other changes which may exist, and which are encompassed by a gene. Applicants have defined the polymorphisms in the context of specific base pair changes in sequences defined by SEQ ID NOs, however have failed to adequately describe the sequences of a gene. Dependent claims 2 and 3 are included in this rejection because they fail to clarify the basis of the rejection.

Conclusion

No claim is allowed. Pending claims are free of the art of record because that art fails to teach the specific genetic polymorphisms in the hMLH1 and hMSH2 genes instantly claimed. However, the claims are subject to other rejections.

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All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.53(d). Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.35(d). See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached at (703)305-6608.

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Any inquiry of a general nature or relating to the status of this application should be directed to Kay Pinkney whose telephone number is (703)306-3076.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Voitach



DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/6.30